REMARKS

Claims 35-52 are pending and under examination. Claims 1-34 and 53-103 stand withdrawn for being directed to a non-elected invention. Applicants' reserve the right to pursue prosecution of thee non-elected claims in a later filed application claiming priority to the subject application. Applicants have reviewed the rejections set forth in the Office Action mailed April 4, 2007, and respectfully traverse all grounds for the reasons that follow.

Double Patenting

Claims 35-52 stand provisionally rejected under the judicially-created doctrine of obvious-type double patenting as allegedly unpatentable over claims 5, 6, 11 and 13-30 of copending application serial no. 10/194,958. Claims 35, 39, 41-44, 47 and 49 stand rejected allegedly for obvious-type double patenting over claims 1-2, 10, 18, 20-24, 32, 39-40, 42-46, 54 and 64-66 of copending application 10/864,935. The Office alleges that, although the conflicting claims are not identical, they are obvious over each because they are drawn to methods containing similar steps. Applicants respectfully request deferral of this provisional rejection until there is an indication of allowable subject matter one or more of the allegedly conflicting applications.

Rejections Under 35 U.S.C. § 103

Claims 35-46 and 49-52 stand rejected over Bhatnagar et al., U.S. Patent No. 5,593,840, in view of Morris et al., U.S. Patent No. 6,017,738, and Barany et al., US2002/0150921. The rejection expressly reiterates the Examiner's reasons provided in the Office Action mailed July 19, 2006, except it cites Barany et al. in lieu of conceding that Bhatnagar et al. fails to disclose a probe having an adapter sequence.

In particular, the Examiner alleges that Bhatnagar et al. describe a process for amplifying a nucleic acid sequence for detection of a point mutation which extends and ligates first and second primers followed by amplification of the product. The Examiner concedes that Bhatnagar et al. do not disclose linear amplification, a first or second universal priming site, an adapter sequence-containing probe or determining a relative amount of first and second amplicons. The Examiner alleges linear amplification is accomplished through extension using a

third primer and that Bhatnagar's extension and/or ligation primers correspond to the claimed universal primers and/or adapter sequences because these elements lack physical features other than binding to a primer for amplification or hybridization. Morris et al. is alleged to describe a method using a solid phase amplification method which incorporates a label using RNA transcription. The Office concludes that it would have been obvious to apply the method of Bhatnagar et al. to determine the relative amount of first and second amplicons allegedly because Morris et al. describe that incorporation of label into amplified nucleic acid sequences allows detection and quantification.

The additional citation to Barany et al. is allegedly cited because Bhatnagar et al. and Morris et al. fail to disclose target sequences having a solid support, immobilization of amplification templates or amplicons to a solid support with a capture probe. In particular, the Examiner alleges that Barany et al. describe a quantitative method for identifying mutations which employs an oligonucleotide having an addressable array-specific portion that can be immobilized on an array following ligation. The Examiner concludes that one of ordinary skill in the art would have been motivated to apply the addressable array-specific portion of Barany et al. to the probe of Bhatnagar et al. because the method provides quantitative detection of mutations in a high background of normal sequences.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 180 U.S.P.Q. 580 (C.C.P.A. 1974); M.P.E.P. §2143.03. Applicants claim a method of detecting the relative amounts of two or more target sequences. As described further below, the cited combination of references fails to teach or suggest this claimed element.

Applicants respectfully draw the Examiner's attention to independent claim 35, which is directed to a method of detecting the relative amounts of two or more target sequences. The method includes hybridizing first and second pairs of ligation probes with first and second target sequences to form first and second ligation complexes; ligating the first and second ligation complexes to form first and second ligated probes; linear amplifying the first and second ligated probes to produce first and second amplicons, and determining the relative amounts of the

amplicons, which indicates the relative amount of the first target sequence to the second target sequence.

By the Examiner's own admission, Bhatnagar et al. does not disclose determining relative amounts of two or more target sequences. The Examiner's withdrawal of the previous rejection over Bhatnagar et al. in view of Morris et al. confirms that the combination of these two references fails to teach or suggest the claimed invention directed to determining the relative amounts of two or more target sequences.

The inclusion of Barany et al. does not cure this deficiency because Barany et al. is cited for allegedly describing use of a probe having an addressable array-specific portion for quantitatively identifying mutations. With respect to independent claim 35, Barany et al. is irrelevant because no immobilization step is claimed. Accordingly, the asserted motivation in Barany et al. to provide quantitative detection of mutations in a high background of normal sequences also is immaterial because this alleged characteristic is directed a solid phase assay, which is not a step recited in independent claim 35.

Therefore, as to independent claim 35, the combination of Bhatnagar et al. in view of Morris et al. and Barany et al. is effectively a rejection applying only Bhatnagar et al. and Morris et al. as applicable art. As Applicants have previously shown on the record and set forth above, the claimed invention is unobvious over Bhatnagar et al. in view of Morris et al. because this rejection has been issued, rebutted and withdrawn. Accordingly, the claimed invention is unobvious over the cited art and withdrawal of this ground of rejection is respectfully requested.

Dependent claims 47 and 48 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Bhatnagar et al., in view of Morris et al. and Barany et al. as applied above and further in view of Akhavan-Tafti, U.S. Patent No. 5,998,175. The Office concedes that Bhatnagar et al., Morris et al. and Barany et al. do not disclose a plurality of more than two pairs of ligation probes with a plurality of more than two target sequences, but alleges that Akhavan-Tafti describes a method of synthesizing polynucleotides using simultaneous ligation of a set of oligomers onto a template bound primer which inherently describes the use of a plurality of more than two pairs of ligation probes. The Office concludes that it would have been obvious to apply

the plurality of pair of ligation probes as claimed allegedly because the method of Akhavan-Tafti can be used to copy DNA or RNA linearly or exponentially.

Claims 47 and 48 depend from and contain all elements of base claim 35. Akhavan-Tafti is cited for allegedly describing more than two pairs of ligation probes and similarly fails to provide the missing teaching or suggestion from the combination of Bhatnagar et al., Morris et al. and Barany et al. to arrive at the claimed method of detecting the relative amounts of two or more target sequences because the synthesis procedure described by Akhavan-Tafti is directed to the ligation of oligomer sets, not to detecting relative amounts of target sequences as claimed. Accordingly, the cited combination fails to render the claimed invention obvious and withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, she is invited to call David Gay.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP

David A. Gay
Registration No. 39,200

4370 La Jolla Village Drive, Suite 700
San Diego, CA 92122
Phone: 858.535.9001 DAG:cjh
Facsimile: 858.597.1585
Date: July 3, 2007

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